

## Claims:

1. A method of assessing a disease condition in an individual comprising;

5       contacting said nucleosomes from a biological fluid sample obtained from the individual with an antibody which binds specifically with a modified histone protein,

          wherein binding of said antibody to said nucleosomes is indicative that the individual has a disease condition.

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2. A method according to claim 1 wherein said nucleosomes are concentrated from the biological fluid sample.

3. A method according to claim 1 or claim 2 wherein the  
15       disease condition is a cancer condition or an autoimmune disease.

4. A method according to any one of the preceding claims wherein the modified histone has a modification shown in Table  
20       1.

5. A method according to any one of the preceding claims wherein the modified histone has a modification shown in Table  
25       2.

6. A method according to any one of the preceding claims wherein said antibody comprises a detectable label.

7. A method of assessing histone modification in nucleosomes  
30       in a biological fluid sample from an individual comprising;  
          contacting a biological fluid sample from said individual with a first antibody,  
          determining binding of said first antibody to a nucleosome containing a histone modification using a second antibody,

wherein one of said first or second antibodies binds to a nucleosome and the other of said first or second antibodies binds specifically to a modified histone.

5 8. A method according to claim 7 wherein said first antibody binds to nucleosomes and the second antibody binds specifically to the modified histone.

9. A method according to claim 7 wherein the second antibody  
10 binds to nucleosomes and the first antibody binds specifically to the modified histone.

10. A method according to any one of claims 7 to 9 wherein the modified histone comprises a modification shown in Table 1.

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11. A method according to any one of claims 7 to 9 wherein the modified histone comprises a modification shown in Table 2.

12. A method wherein according to any one of claims 7 to 11  
20 the biological fluid sample is a plasma or serum sample.

13. A method according to any one of claims 7 to 12 wherein said first or said second antibody is immobilised.

25 14. A method according to claim 13 wherein the non-immobilised antibody of said first and second antibodies comprises a detectable label.

15. A method of assessing histone modification in cell-free  
30 nucleosomes in a biological fluid sample comprising;  
contacting a biological fluid sample with an antibody which binds specifically to a histone comprising a modification, determining the binding of said antibody to nucleosomes in said sample,

the binding of said antibody being indicative of the presence of modified histone in nucleosomes in the blood of said individual.

5 16. A method according to claim 15 wherein the modification is a modification shown in Table 1.

17. A method according to claim 15 or claim 16 wherein the modification is a modification shown in Table 2.

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18. A method according to any one of claims 15 to 17 wherein the disease condition is a cancer condition or an autoimmune disease.

15 19. A method according to any one of claims 15 to 18 wherein said antibody comprises a detectable label.

20. A method of diagnosing a cancer condition in an individual comprising;

20 contacting biological fluid sample obtained from an individual with an antibody which binds specifically to a modified histone,

determining the binding of said antibody to nucleosomes in said sample,

25 the binding of said antibody to nucleosomes in said sample being indicative that said individual has a cancer condition.

21. A method according to claim 20 wherein the disease  
30 condition is a cancer condition or an autoimmune disease.

22. A method according to claim 20 or claim 21 wherein the modified histone has a modification shown in Table 1.

35 23. A method according to any one of claims 20 to 22 wherein the modified histone has a modification shown in Table 2

24. A method according to any one of claims 20 to 23 wherein said modification is not H2B Ser 14 (P).

25. A method according to any one of claims 20 to 24 wherein  
5 said antibody comprises a detectable label.

26. A method according to any one of claims 1 to 25 comprising isolating DNA associated with the nucleosome comprising a modified histone.

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27. A method according to claim 26 comprising amplifying said nucleosome associated DNA.

28. A method according to claim 26 or claim 27 comprising  
15 sequencing said nucleosome associated DNA.

29. A method according to any one of claims 26 to 28 comprising labelling said nucleosome associated DNA with a detectable label.

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30. A method according to any one of claims 26 to 29 comprising contacting said nucleosome associated DNA with a DNA molecule having a known sequence under conditions suitable for hybridisation and determining hybridisation.

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31. A method according to claim 30 wherein said DNA molecule of known sequence is comprised in a microarray.

32. A method according to any one of claims 26 to 31 claim  
30 comprising determining the hybridisation of DNA from said individual which is associated with said histone modification relative to DNA associated with said histone modification from one or more other individuals.

33. A method according to any one of claims 26 to 31 wherein said modified histone comprises a modification associated with gene silencing.

5 34. A method according to claim 33 wherein said modification is selected from H3 Lys 9 (Me), H3 Lys 27(Me), H3 Lys 36(Me), H3 Lys 79(Me) and H4 Lys 20(Me).

10 35. A method according to any one of claims 26 to 34 wherein said modified histone comprises a modification associated with gene activation.

15 36. A method according to claim 35 wherein said modification is selected from H3 Lys 4 (Me), H3 Lys 9(Ac), H3 Lys 14(Ac) and H3 Lys 23(Ac).

37. A method of identifying a tumour suppressor gene comprising;

20 contacting biological fluid sample obtained from an individual suffering from a cancer condition with an antibody which binds specifically to a histone having a modification associated with silencing,

25 isolating nucleosomes bound to said antibody, sequencing DNA associated with said bound nucleosomes, and;

identifying said DNA as a tumor suppressor gene.

38. A method according to claim 37 wherein said modification is selected from H3 Lys 9 (Me) H3 Lys 27(Me), H3 Lys 36(Me), H3 30 Lys 79(Me) and H4 Lys 20(Me).

39. A method of identifying an oncogene comprising;

35 contacting biological fluid sample obtained from an individual suffering from a cancer condition with an antibody which binds specifically to a histone having a modification associated with activation,

isolating nucleosomes bound to said antibody,  
sequencing DNA associated with said bound nucleosomes,  
and;  
identifying said DNA as an oncogene.

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40. A method according to claim 39 wherein said modified histone comprises a modification shown in Table 1 and/or Table 2.

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41. A method of identifying a patient as a responsive to histone modification modulation therapy comprising;  
determining the level of histone modification in cell-free nucleosomes within a sample obtained from the patient, relative to a sample obtained from a healthy individual,  
15 a change in the level of modification being indicative that the patient is responsive to histone modification modulation therapy.

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42. A method of assessing a patient for a therapeutic treatment comprising;  
determining the presence of one or more genes which confer resistance to said treatment in cell-free nucleosomes in a sample obtained from the patient,  
wherein said nucleosomes comprise a histone modification  
25 associated with activation.

43. A method according to claim 42 wherein said modification is a modification shown in Table 1 and/or Table 2.

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44. A method of determining the presence of a cell-free nucleosome having a histone modification comprising;  
determining the presence of an antibody which binds specifically to the histone modification in a sample obtained from an individual,

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the presence of said antibody being indicative of the presence of said nucleosomes in said individual.

45. A method according to claim 44 comprising contacting the sample with an antigen comprising a histone modification epitope and determining binding to the antigen.

5 46. A method according to claim 45 wherein said antigen is immobilised on a solid support.

47. A method according to claim 45 wherein said antigen comprises a detectable label.

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48. A method according to any one of claims 44 to 47 wherein said modified histone comprises a modification shown in Table 1 and/or Table 2.

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